



A Pilot Study to Select a Dose of Naltrexone Hydrochloride that Will Reduce Subjective Euphoric Effects of Oxycodone Hydrochloride in Non-Dependent, Opioid-Preferring Subjects

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Introduction

- Prescription drug abuse has reached an alarming rate in America. Reward seekers have found formulations like OxyContin easy to manipulate to obtain a large release of the active pharmaceutical agent.
- New formulations are being explored in an effort to find ways to deter the abuse of opioids.
- One approach is to design a product that would release an opioid antagonist if the formulation were altered, blocking the euphoric effect and thus eliminating the reason to alter the formulation.

Objective

- To determine the dose of oral naltrexone hydrochloride (HCL) that will reduce the "liking" scale of the Drug Evaluation Questionnaire (DEQ) when administered with oral oxycodone HCL.

Methods

- Eighty-two males, 18 to 50 years, who had abused opioids on at least 5 occasions within 12 months but were not physically dependent on opioids, were randomized to receive a combined dose of oxycodone HCL and naltrexone HCL.

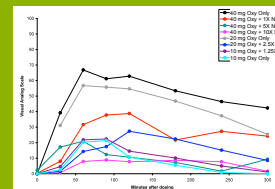
Methods

- Four groups received 40 mg oxycodone with individual groups receiving 0, 1X, 5X, or 10X naltrexone.
- One group received 20 mg oxycodone with 2.5X naltrexone; and two groups received 10 mg of oxycodone: one with 0 naltrexone and one with 1.25X naltrexone.
- Subjects completed the following measures at selected times from pre-dose to 5 hours post treatment: The Drug Evaluation Questionnaire (DEQ), consisting of 9 items related to drug effects rated from 0 = None to 100 = Extremely; and the Morphine Benzadrine Group (ARCI-MBG) Scale, consisting of 16 items rated on a scale from 0 = False to 3 = True.

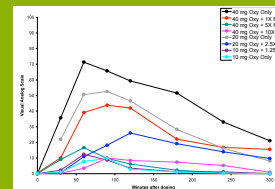
Results

- At 40 mg of oxycodone, 5X and 10X naltrexone showed significantly lower DEQ and MBG scores compared to 0 naltrexone. The 1X dose showed lower scores for only a few test items.
- At 20 mg of oxycodone, 2.5X naltrexone showed significant decreases from 0 naltrexone for DEQ items 1, 2, 4, and 5 and the MBG total score. No discrimination was found between 0 and 1.25X naltrexone at 10 mg of oxycodone.

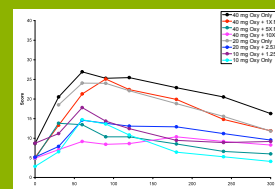
Summary DEQ #4: Do You Like the Drug?



Summary DEQ #5: How High Are You Now?



MBG Total Scores



Discussion

- This study shows a dose-response reduction of opioid-induced euphoria (DEQ question 5) from naltrexone in non dependent but opioid-preferring subjects. This type of study has not been previously reported. The ability to titrate the reduction in the rewarding effects of an opioid suggests that a ratio of an opioid antagonist to an agonist may be a useful property of an opioid formulation to reduce the risk of opioid abuse.
- Two standard assessment tools to measure the rewarding effect from opioids are the DEQ and the MBG. DEQ questions 4 and 5 assess different properties of a drug. Drug-induced euphoria is best assessed by DEQ question 5. It is notable that no discrimination was found between 10 mg of oxycodone with or without naltrexone. This suggests that 10 mg of oxycodone could not produce sufficient euphoria for naltrexone to block.
- Further studies will be required to determine the analgesic and withdrawal effects of the ratio of naltrexone to oxycodone used in this study if naltrexone is released with chronic opioid therapy.

Conclusion

- Naltrexone was found to have a dose-dependent reduction on the euphoric ("liking") effect of oxycodone, suggesting potential value in formulating naltrexone-oxycodone abuse-deterrent analgesics. The effective dose of naltrexone appears to be a ratio that can be dialed in to reduce euphoria to 0. The reducing ratio was similar at 40 mg and 20 mg oxycodone.